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L8: Entry 2 of 4

File: JPAB

Jul 25, 1995

PUB-NO: JP407187989A

DOCUMENT-IDENTIFIER: JP 07187989 ATITLE: EXTRACTED SOLUTION OF PERILLA FRUTESCENS AND SKIN-BEAUTIFYING COSMETIC
CONTAINING THE SAME

PUBN-DATE: July 25, 1995

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APPL-NO: JP05348476

APPL-DATE: December 27, 1993

INT-CL (IPC): A61 K 7/48; A61 K 7/00; A61 K 7/42; A61 K 35/78

ABSTRACT:

PURPOSE: To obtain an extracted solution of Perilla frutescens containing rosmarinic acid, etc., as a pharmacodynamic component of a labiate plant in a high concentration but hardly a dark yellowish brown, greenish brown or reddish brown coloring matter as a characteristic of Perilla frutescens and to provide a new and industrially advantageous production method therefor.

CONSTITUTION: A labiate plant is extracted with a lower alcohol having 10-30vol.% water content and water is added to the extracted solution to removed formed precipitate. The prepared extracted solution is concentrated, mixed with a lower alcohol to give ≥ 90 vol.% alcohol concentration, formed precipitated is removed and a liquid component is obtained again to provide a method for producing an extracted solution of Perilla frutescens. A melanism inhibitor comprises the extracted solution of Perilla frutescens and a skin- beautifying cosmetic contains the extracted solution of Perilla frutescens. The extracted solution of Perilla frutescens has high safety to human and is usable as a stable melanism inhibitor.

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First Hit

L1: Entry 7 of 8

File: DWPI

Jul 25, 1995

DERWENT-ACC-NO: 1995-290282

DERWENT-WEEK: 199921

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TITLE: Perilla extract used for skin whitening cosmetic - prepd by extracting Perilla with lower alcohol, adding water, condensing extracted soln, and removing ppte

PATENT-ASSIGNEE:

ASSIGNEE

CODE

NAGASE SANGYO KK

NAGS

PRIORITY-DATA: 1993JP-0348476 (December 27, 1993)

Search Selected

Search ALL

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PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
<input type="checkbox"/> JP 07187989 A	July 25, 1995		006	A61K007/48
<input type="checkbox"/> JP 2884466 B2	April 19, 1999		006	A61K007/48

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
JP 07187989A	December 27, 1993	1993JP-0348476	
JP 2884466B2	December 27, 1993	1993JP-0348476	
JP 2884466B2		JP 7187989	Previous Publ.

INT-CL (IPC): A61 K 7/00; A61 K 7/42; A61 K 7/48; A61 K 35/78

ABSTRACTED-PUB-NO: JP 07187989A

BASIC-ABSTRACT:

Perilla extract, its prepn. method and its use for whitening cosmetic alcohol with 10-30 vol.% moisture content, adding water to remove the ppte., condensing the extracted soln., adding lower alcohol to adjust the alcohol conc. to more than 90 vol.% and removing the ppte. to collect the liq. component, or (b) extracting Perilla plants with lower alcohol with 10-30 vol.% moisture content, condensing the extracted soln., adding water to adjust the alcohol concn. to up to 10 vol.%, removing the ppte., condensing the extracted soln., adding alcohol to adjust the alcohol concn. to up to 90 vol.%, removing the ppte. to collect the liq. component, and removing the impurity by adding active charcoal.

Pref., perilla plants are pref. *Perilla frutescens* Britton var. *acuta* Kudo, *Perilla frutescens* Britton var. *acuta* Kudo form *viridis* Makino, *Perilla frutescens* Britton var. *crispa* Decne or *Romarinus officinalis*.

USE/ADVANTAGE - The Perilla extract is used as a melanin generation inhibitor and cosmetic for whitening the skin (claimed). The melanin generation inhibitor is used for prevention of pigmentation and sunburn and for whitening the skin. The extract is safe and stable. It inhibits tyrosinase activity.

In an example, skin lotion comprised 4.0 wt.% conc. glycerine, 4.0 wt.% sorbit soln., citric acid, 0.3 wt.% sodium citrate, 0.5 wt.% polyoxyethylene hardened castor oil, 15.0 wt.% ethanol, 1.0 wt.% Perilla extract, 0.05 wt.% fragrance and balance distilled water.

CHOSEN-DRAWING: Dwg.0/0

TITLE-TERMS: PERILLA EXTRACT SKIN WHITE COSMETIC PREPARATION EXTRACT PERILLA LOWER ALCOHOL ADD WATER CONDENSATION EXTRACT SOLUTION REMOVE PRECIPITATION

DERWENT-CLASS: B04 D21

CPI-CODES: B04-A08C2; B04-A10; B14-D08; B14-N17; D08-B09;

CHEMICAL-CODES:

Chemical Indexing M1 *01*

Fragmentation Code

M423 M720 M903 N161 P923 Q262 V400 V404 V406

SECONDARY-ACC-NO:

CPI Secondary Accession Numbers: C1995-130501

PATENT ABSTRACTS OF JAPAN

(11)Publication number : **07-187989**

(43)Date of publication of application : **25.07.1995**

(51)Int.Cl.

A61K 7/48

A61K 7/00

A61K 7/42

A61K 35/78

(21)Application number : **05-348476**

(71)Applicant : **NAGASE & CO LTD**

(22)Date of filing : **27.12.1993**

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OSANAI YUUKO**

(54) EXTRACTED SOLUTION OF PERILLA FRUTESCENS AND SKIN-BEAUTIFYING COSMETIC CONTAINING THE SAME

(57)Abstract:

PURPOSE: To obtain an extracted solution of *Perilla frutescens* containing rosmarinic acid, etc., as a pharmacodynamic component of a labiate plant in a high concentration but hardly a dark yellowish brown, greenish brown or reddish brown coloring matter as a characteristic of *Perilla frutescens* and to provide a new and industrially advantageous production method therefor.

CONSTITUTION: A labiate plant is extracted with a lower alcohol having 10-30vol.% water content and water is added to the extracted solution to removed formed precipitate. The prepared extracted solution is concentrated, mixed with a lower alcohol to give ≥ 90 vol.% alcohol concentration, formed precipitated is removed and a liquid component is obtained again to provide a method for producing an extracted solution of *Perilla frutescens*. A melanism inhibitor comprises the extracted solution of *Perilla frutescens* and a skin-beautifying cosmetic contains the extracted solution of *Perilla frutescens*. The extracted solution of *Perilla frutescens* has high safety to human and is usable as a stable melanism inhibitor.

LEGAL STATUS

[Date of request for examination]

16.12.1996

[Date of sending the examiner's decision of

rejection]

[Kind of final disposal of application other than
the examiner's decision of rejection or
application converted registration]

[Date of final disposal for application]

[Patent number] 2884466

[Date of registration] 12.02.1999

[Number of appeal against examiner's
decision of rejection]

[Date of requesting appeal against examiner's
decision of rejection]

[Date of extinction of right]

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CLAIMS

[Claim(s)]

[Claim 1] the beefsteak plant characterized by adding lower alcohol, carrying out to more than alcoholic concentration 90 volume %, removing the precipitate to produce, and obtaining a liquefied component again after the lower alcohol of water content 10 - 30 volume % extracting the Lamiaceae vegetation, removing the precipitate which adds water and is produced and condensing the obtained extract -- the manufacture approach of an extract.

[Claim 2] After the lower alcohol of water content 10 - 30 volume % extracting the Lamiaceae vegetation and condensing the obtained extract, Add water and the precipitate which makes alcoholic concentration below 10 volume %, and is produced is removed. after condensing the obtained extract, lower alcohol is added, it carries out to more than alcoholic concentration 90 volume %, the precipitate to produce is removed, and a liquefied component is obtained again, and activated carbon is added further and it remains -- impure -- a part -- the beefsteak plant characterized by removing -- the manufacture approach of an extract.

[Claim 3] the beefsteak plant according to claim 1 or 2 whose Lamiaceae vegetation is a beefsteak plant, AOJISO, dust MENJISO, or a rosemary -- the manufacture approach of an extract.

[Claim 4] the beefsteak plant obtained by adding lower alcohol, carrying out to more than alcoholic concentration 90 volume %, and removing the precipitate to produce after the lower alcohol of water content 10 - 30 volume % extracting the Lamiaceae vegetation, removing the precipitate which adds water and is produced and condensing the obtained extract -- the melanin generation inhibitor which consists of an extract.

[Claim 5] After the lower alcohol of water content 10 - 30 volume % extracting the Lamiaceae vegetation and condensing the obtained extract, Add water and the precipitate which makes alcoholic concentration below 10 volume %, and is produced is removed. after condensing the obtained extract, lower alcohol is added, it carries out to more than alcoholic concentration 90 volume %, the precipitate to produce is removed, and a liquefied component is obtained again, and activated carbon is added further and it remains -- impure -- a part -- the beefsteak plant obtained by removing -- the melanin generation inhibitor which consists of an extract.

[Claim 6] The melanin generation inhibitor according to claim 4 or 5 whose Lamiaceae vegetation is a beefsteak plant, AOJISO, dust MENJISO, or a rosemary.

[Claim 7] the beefsteak plant obtained by adding lower alcohol, carrying out to more than alcoholic concentration 90 volume %, and removing the precipitate to produce after the lower alcohol of water content 10 - 30 volume % extracting the Lamiaceae vegetation, removing the precipitate which adds water and is produced and condensing the obtained extract -- the whitening cosmetics characterized by containing an extract.

[Claim 8] After the lower alcohol of water content 10 - 30 volume % extracting the Lamiaceae vegetation and condensing the obtained extract, Add water and the precipitate which makes alcoholic concentration below 10 volume %, and is produced is removed. after condensing the obtained extract, lower alcohol is added, the precipitate which carries out to more than alcoholic concentration 90 volume

%, and is produced is removed, and a liquefied component is obtained again, and activated carbon is added further and it remains -- impure -- a part -- the beefsteak plant obtained by removing -- the whitening cosmetics characterized by containing an extract.

[Claim 9] Whitening cosmetics according to claim 7 or 8 whose Lamiaceae vegetation is a beefsteak plant, AOJISO, dust MENJISO, or a rosemary.

[Translation done.]

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DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Industrial Application] a beefsteak plant with this invention effective in prevention and clearance of chromatosis, such as whitening of the skin or suntan, and silverfish, buckwheat dregs, -- the beefsteak plant which hardly contains a coloring matter component peculiar to a beefsteak plant about the manufacture approach of an extract although a ROZUMARIN acid etc. is contained in high concentration in detail and which is used suitable for whitening cosmetics -- it is related with the manufacture approach of an extract. furthermore, the beefsteak plant -- it is related with the whitening cosmetics containing it about the application using an extract as a melanin generation inhibitor effective in prevention and clearance of chromatosis, such as whitening of the skin or suntan, and silverfish, buckwheat dregs.

[0002]

[Description of the Prior Art] Conventionally, the method of obtaining an extract using the carbon dioxide of hot water or a liquid region is examined from the Lamiaceae vegetation (JP,62-65660,A, JP,60-120957,A). However, these approaches aim at obtaining without mainly harming a coloring matter component peculiar to a beefsteak plant, or an aroma component, and since coloring matter peculiar to a beefsteak plant, sugar, tannin, etc. are contained so much, such an extract presents a very deep yellowish brown color, greenish-brown, or dark reddish-brown, and has the peculiar odor. When such an extract is blended with the charge of makeup, or skin external preparations, the problem on pharmaceutical preparation, such as coloring and destabilization of an emulsification system, arises, and there is inconvenience that the pharmaceutical form and loadings are restrained considerably.

[0003] By the way, it is already known that a ROZUMARIN acid has the pharmacology effectiveness, such as anti-inflammatory activity and an antiallergic operation, as an active principle of the Lamiaceae vegetation, such as a beefsteak plant, AOJISO, dust MENJISO, a rosemary (rosemary) that is one sort of a herb, a peppermint, KAWAMIDORI, and prolongation-of-life grass, and these vegetation is used as a folk medicine with safety high for many years. Therefore, the extract which extracted the above-mentioned Lamiaceae vegetation with hot water etc. is although the ROZUMARIN acid is contained, Even if it is going to blend such an extract with the charge of makeup, or skin external preparations and is going to use the drug effect of a ROZUMARIN acid, it is difficult to carry out the addition activity of the extract by the high concentration which there is a problem on pharmaceutical preparation, such as coloring originating in the above-mentioned contaminant and destabilization of an emulsification system, therefore the loadings of an extract have constraint, and fully does so the drug effect as a ROZUMARIN acid in the charge of makeup, or skin external preparations.

[0004] Although the approach of carrying out extract purification of the ROZUMARIN acid in the purest possible form from the Lamiaceae vegetation, and applying to the charge of makeup is proposed based on such a background (JP,63-162611,A), the extract process using dangerous solvents, such as an acetone and ethyl ether, the process of column chromatography purification, etc. are quite complicated, and special equipment is required for them, and they are not advantageous as the extract purification

approach from the Lamiaceae vegetation. [of the operating instructions]

[0005] By the way, the pigmentation of the skins, such as suntan, and silverfish, buckwheat dregs, is produced by the coloring matter melanin generated in the cell melanocyte which exists in an epidermal cell being spread into a contiguity cell. Various drugs which control melanin generation by controlling generation of the enzyme tyrosinase which has played the central role in melanin generation with this melanocyte, or checking an enzyme tyrosinase directly are known. There are kojic acid and arbutin as typical drugs used conventionally. Moreover, from the dopa produced according to an operation of an enzyme tyrosinase, or a dopa quinone, although melanin generates by the nonenzymatic oxidation, various drugs like an enzyme or which control the generation are also known for checking the process. There are an ascorbic acid, hydroquinone, etc. as the typical drugs. However, these melanin generation inhibitors cannot necessarily be satisfied as a charge raw material of makeup, when taking into consideration the toxicity and skin sensuous effect to *Homo sapiens*, stability, etc. Therefore, it is extremely stable and development of a stable melanin generation inhibitor is desired.

[0006]

[Problem(s) to be Solved by the Invention] An example is taken by the trouble on the pharmaceutical preparation generated when blending an extract with the charge of makeup, or skin external preparations, the trouble for extract purification, etc. as mentioned above, the conventional beefsteak plant -- the object of this invention A beefsteak plant [*Perilla frutescens*(L.) Britton var. *acuta* Kudo], AOJISO [*Perilla frutescens*(L.) Britton var. *acuta* Kudo formaviridis Makino], Dust MENJISO [*Perilla frutescens*(L.) Britton var. *crispa*(Thunb.) Decne], The caffeine acid of the drug effect component of the Lamiaceae vegetation, such as a rosemary [a rosemary and *Rosmarinus officinalis*], the beefsteak plant which contains perillaldehyde, a ROZUMARIN acid, etc. in high concentration, and moreover hardly contains the coloring matter of a deep yellowish brown color peculiar to a beefsteak plant, greenish-brown, or dark reddish-brown -- it is in the new thing for which the advantageous manufacture approach is offered industrially with an extract. the beefsteak plant which can be used as a melanin generation inhibitor which whose safety to *Homo sapiens* was high collectively, and was extremely excellent -- it is in offering an extract.

[0007]

[Means for Solving the Problem] the beefsteak plant which has the following processes in order that this invention person may solve the above technical problem -- the manufacture approach of an extract -- being established -- the beefsteak plant -- the extract had the operation which checks generation of an enzyme tyrosinase, and safety began and found out that it could use as a stable high melanin generation inhibitor, and completed this invention.

[0008] Namely, according to this invention, the lower alcohol of water content 10 - 30 volume % extracts the Lamiaceae vegetation. After condensing the obtained extract below to 10 volume %, add water and the precipitate which makes alcoholic concentration below 10 volume %, and is produced is removed. Again, after condensing below to 10 volume %, add lower alcohol and the obtained extract is carried out to more than alcoholic concentration 90 volume %. the precipitate which deposits is removed, liquefied components are collected again, and an extract is obtained, and activated carbon is added further, and it stirs and remains -- impure -- a part -- the beefsteak plant made into the object by removing -- an extract can be obtained. this beefsteak plant -- safety of an extract can be high, can use it for the application as a stable melanin generation inhibitor, and can blend it with whitening cosmetics.

[0009] As Lamiaceae vegetation used by this invention, a beefsteak plant, AOJISO, dust MENJISO, a rosemary (rosemary), etc. are mentioned in more detail. Moreover, it considers as the vegetable part containing many active principles which have melanin generation inhibitory action, and there is the leaves-and-stems section. You may use with extraction happiness in the next life, and even if it uses what carried out desiccation processing of solar drying etc., it does not interfere. As for leaves and stems, it is desirable on extraction efficiency to use what was made into the shape of a split. It does not interfere, even if perillae folium is marketed as a crude drug and it uses this as a desiccation article of dust MENJISO.

[0010] Although it is sufficient for it if the amount of the lower alcohol of the water content 10 - 30

volume % which extract a component, i.e., water alcohol, is an amount in which leaves and stems are immersed, its five to 15 time weight of the Lamiaceae vegetation is desirable. When using non-dried vegetation, it is desirable to set up the alcoholic concentration of an extracting solvent more highly in consideration of the moisture in vegetation. Ethanol and a methanol are preferably good although there are a methanol, ethanol, n-propanol, isopropanol, a t-butanol, etc. as lower alcohol. If the water content of an extracting solvent separates from 10 - 30 volume %, it is contaminated with the component and coloring matter which are not made into the object.

[0011] Although extract operation may be performed at a room temperature, if it heats under reflux cooling preferably, a melanin generation control component will be extracted promptly efficiently.

***** is good at ordinary pressure, and although extract time amount changes with extract temperature, 2 - 48 hours is desirable. Insoluble residue is filtered and removed after extract operation. If extract operation of a component is repeatedly performed also about residue, it can raise yield. After condensing until it becomes below 10 volume % of the volume of the extract of being also with a vacuum concentration machine about the obtained extract, subsequently water is added, alcoholic concentration is made below into 10 volume %, and filtration etc. removes the precipitate which puts for 15 hours or more and is preferably produced at 4-10 degrees C. Again, lower alcohol after condensing below to 10 volume % is added, the extract which is the obtained liquefied component is carried out to more than alcoholic concentration 90 volume %, filtration etc. removes the precipitate which puts for 15 hours or more and deposits at 4-10 degrees C preferably, liquefied components are collected again, and an extract is obtained. to this extract, 0.5 - 2% of the weight of activated carbon is added, and it stirs and remains -- impure -- a part -- the beefsteak plant which is removed and is made into the object -- an extract is obtained. thus, the obtained beefsteak plant -- it became clear by the qualitative test that an extract contains matter, such as a caffeine acid, perillaldehyde, and a ROZUMARIN acid. moreover, a beefsteak plant -- this invention person begins for an extract to have melanin generation inhibitory action, and it finds out.

[0012]

[Example 1] a beefsteak plant -- 80 volume % ethanol (water content 20 volume %) 600L was added to the 50kg (UCHIDA ****) of the manufacture approach perillae folium of an extract, and standing and an immersion extract were performed at 40 degrees C under warming for 24 hours. The 80 volume % ethanol of 600L was added to the pan after filtering an extract at the perillae folium of residue, and same actuation was carried out. The extract (primary extract) of 1097 in all L was obtained for 2 times of extracts. this primary extract -- 50 degrees C -- warming -- after carrying out bottom vacuum concentration and making it 50L, water 100L was added and it put at 10 degrees C for 24 hours. After carrying out filtration clearance of the produced insoluble precipitate, adding 0.75 % of the weight of activated carbon and carrying out stirring processing for 1 hour, this was removed by filtration. filtration residue -- further -- the 90 volume % ethanol of 3L -- washing -- the beefsteak plant of 102 in all L -- the extract was obtained. the beefsteak plant from this perillae folium -- according to the tyrosinase activity measurement trial of an example 2, an extract is a fraction which shows melanin generation control inhibitory action. (that tyrosinase activity measurement trial -- setting -- this beefsteak plant -- an extract -- -- a beefsteak plant -- it uses as extract".)

[0013]

[Example 2] It is the melanoma (melanoma) cell B16 share of the tyrosinase activity effectiveness mouse origin 150cm² In the flask for animal culture which contains 30ml of MEM culture media of fetal-calf-serum content 10% The cell density is 2.5x10⁴. A cell / cm² It inoculates so that it may become, and it is 5%CO₂. The bottom, the matter shown in the following table 1 after 24-hour culture at 37 degrees C was added in each flask so that it might become declared operation concentration, and culture was further performed for three days under these conditions.

[0014] It processed with the trypsin solution 0.25% after culture termination, cells were collected, 10ml of PBS (-) buffer solutions washed twice, and it suspended after that in 2ml (pH6.8) of 0.1% Triton X100 content 0.1M phosphate buffer solutions. After sonication, centrifugal was carried out for 20 minutes in 12000rpm, and the supernatant was obtained and it considered as the tyrosinase fraction.

[0015] 0.5ml (pH6.8) of L-DOPA content phosphate buffer solutions was mixed with 0.5ml of tyrosinase fractions 0.05%, the absorbance of 475nm was measured with time at the room temperature, and tyrosinase activity was searched for from the initial velocity. Moreover, the total protein content contained in the tyrosinase fraction is Bio-Rad. Protein It measured according to the manual of Assay (Bio-Rad make).

[0016]

[A table 1]

表 1 チロシナーゼ生成阻害活性

測定薬剤	作用濃度 μg/ml	チロシナーゼ活性 ΔOD ₄₇₅ /min./mg Protein	阻害率 %	メラニン含量 OD ₄₀₀ /l × 10 ⁴ cells	メラニン生成率 %
コントロール		5.748 × 10 ⁻³	0	1.0320	100
アルブチン	10	1.399 × 10 ⁻³	75.7	0.0210	60.2
	30	6.662 × 10 ⁻³	88.4	0.5050	48.9
コウジ酸	200	9.358 × 10 ⁻⁴	83.7	0.0025	87.5
	400	2.880 × 10 ⁻⁴	95.8	0.6440	62.4
シンソ抽出液	3.0	3.618 × 10 ⁻³	37.1	0.5085	48.8
	6.0	2.221 × 10 ⁻³	61.4	0.6470	38.4

[0017] the beefsteak plant extracted by this invention -- an extract has the operation which checks generation of the enzyme tyrosinase which has played the central role in melanin generation with melanocyte, and it is shown by the tyrosinase activity measurement trial of a table 1 that melanin generation is controlled by the operation. As compared with arbutin and kojic acid, the operation is very low concentration and is specific at the point which shows the high rate of tyrosinase inhibition, and a low melanin yield. The extract extracted by the manufacture approach same about a rosemary showed melanin generation inhibitory action similarly.

[0018]

[Example 3] the beefsteak plant of the facial-cleansing-cream example 1 -- an extract is used for the formula (all -- 100 % of the weight) of the following facial cleansing cream as a melanin generation inhibitor.

Component A A weight % myristic acid 14.0 Stearin acid 12.0 Lauric acid 3.5 Oleyl alcohol 1.5 Palm-oil-fatty-acid amide propyl betaine 10.5 Component B Weight % concentrated glycerin 18.0 Potassium hydroxide 7.0 Purified water Remainder Antiseptics (paraoxybenzoic acid) optimum dose Component C weight % -- a beefsteak plant -- extract 0.5 Perfume The heating dissolution of the 0.2 component A is carried out, and it holds at 80 degrees C. The component B which carried out the heating dissolution is independently added to 80 degrees C at Component A, and it mixes enough. It cooled stirring, Component C was added at 50 degrees C, and facial cleansing cream was obtained.

[0019]

[Example 4] the beefsteak plant of the face toilet example 1 -- an extract is used for the formula (all -- 100 % of the weight) of the following face toilet as a melanin generation inhibitor.

A component Weight % purified water Remainder Concentrated glycerin 4.0 Sorbitol liquid (70-% of the weight water solution) 4.0 Citric acid (pH regulator) Optimum dose Sodium citrate 0.3

Polyoxyethylene hydrogenated castor oil 0.5 Ethanol 15.0 a beefsteak plant -- extract 1.0 Perfume It stirred and mixed at the room temperature, all 0.05 components were used as the uniform solution, it adjusted to pH5.5, and face toilet was obtained.

[0020]

[Example 5] the beefsteak plant of the milky lotion example 1 -- an extract is used for the formula (all -- 100 % of the weight) of the following milky lotion as a melanin generation inhibitor.

Component A Weight % purified water Remainder Sucrose fatty acid ester 1.0 (Dai-Ichi Kogyo Seiyaku S-160) Concentrated glycerin 6.0 Antiseptics (paraoxybenzoic acid) Optimum dose Carboxyvinyl polymer 0.06 Potassium hydroxide 0.028 Component B Weight % olive oil 4.0 Jojoba oil 4.0 Lactic-acid Millis Chill 2.0 Self-emulsification mold glyceryl monostearate 1.5 Lipophilic type glyceryl monostearate 1.5 Component C weight % -- a beefsteak plant -- extract 0.5 perfume The heating dissolution of the 0.2 component A is carried out, and it holds at 80 degrees C. The component B which carried out the heating dissolution is independently added to 80 degrees C at Component A, and it mixes enough. It cooled stirring, Component C was added at 50 degrees C, and the milky lotion was obtained.

[0021]

[Example 6] the beefsteak plant of the cream example 1 -- an extract is used for the formula (all -- 100 % of the weight) of the following cream as a melanin generation inhibitor.

Component A Weight % purified water Remainder Concentrated glycerin 6.0 1, 3-butylene glycol 2.0 Antiseptics (paraoxybenzoic acid) Optimum dose Carboxyvinyl polymer 0.22 Potassium hydroxide 0.15 Component B Weight % squalane 7.0 Olive oil 10.0 Jojoba oil 5.0 Self-emulsification mold glyceryl monostearate 1.5 Lipophilic type glyceryl monostearate 1.5 Polysorbate 60 1.8 Monostearin acid sorbitan 0.5 Component C weight % -- a beefsteak plant -- extract 1.5 Perfume The heating dissolution of the 0.2 component A is carried out, and it holds at 80 degrees C. The component B which carried out the heating dissolution is independently added to 80 degrees C at Component A, and it mixes enough. It cooled stirring, Component C was added at 50 degrees C, and the cream was obtained.

[0022] as mentioned above, the beefsteak plant obtained from the Lamiaceae vegetation -- an extract is blended with charges of makeup, such as facial cleansing cream, face toilet, a milky lotion, and a cream, as a whitening component. As a result of applying the charge of makeup to Homo sapiens, the sensuous effect to the skin was very good.

[0023]

[Effect of the Invention] Although anti-inflammatory activity, the antiallergic operation, the spasmodic, an analgesic action, etc. were known by the component of the Lamiaceae vegetation and it was used for it as a folk medicine for many years, it was not known until now that it has an operation of prevention and clearance of chromatinosis, such as whitening of the skin, suntan, and silverfish, buckwheat dregs, and melanin generation control. the beefsteak plant obtained by this invention -- although an extract contains components, such as a caffeic acid, perillaldehyde, and a ROZUMARIN acid, it has the operation which controls generation of the enzyme tyrosinase which has played the central role in coloring matter melanin generation in the cell melanocyte which exists in an epidermal cell, and became clear [that melanin generation is controlled by the operation] from the result of a tyrosinase activity measurement trial of a table 1. therefore, this beefsteak plant -- the extract is very useful as being not only desirable but a melanin generation inhibitor from the point of that safety, and the charge of makeup containing it has the outstanding whitening effectiveness.

[Translation done.]

(19) 日本国特許庁 (J P)

(12) 公開特許公報 (A)

(11) 特許出願公開番号

特開平7-187989

(43) 公開日 平成7年(1995)7月25日

(51) Int. Cl. ⁶	識別記号	庁内整理番号	F I	技術表示箇所
A 6 1 K 7/48				
7/00	K			
	X			
7/42				
35/78	ADA Q	8217-4C		

審査請求 未請求 請求項の数9 F D (全 6 頁)

(21) 出願番号 特願平5-348476

(22) 出願日 平成5年(1993)12月27日

(71) 出願人 000214272

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(54) 【発明の名称】 シソ抽出液、その製造方法およびそれを含有する美白化粧品

(57) 【要約】

【目的】 本発明の目的は、シソ科植物の薬効成分のロズマリン酸等を高濃度に含有するが、シソ特有の濃い黄褐色、緑褐色あるいは赤褐色の色素を殆ど含有しないシソ抽出液と、その新規な工業的に有利な製造方法を提供することにある。併せて、ヒトに対する安全性が高く、安定なメラニン生成阻害剤として用いることのできるシソ抽出液を提供することにある。

【構成】 シソ科植物を含水率10～30体積%の低級アルコールで抽出し、水を加えて生じる沈殿を除去し、得られた抽出液を濃縮後、低級アルコールを加えてアルコール濃度90体積%の以上とし、生じる沈殿を除去して再度液状成分を得ることを特徴とする、シソ抽出液の製造方法、そのシソ抽出液からなるメラニン生成阻害剤、および、そのシソ抽出液を含有する美白化粧品。

【特許請求の範囲】

【請求項1】 シソ科植物を含水率10～30体積%の低級アルコールで抽出し、水を加えて生じる沈殿を除去し、得られた抽出液を濃縮後、低級アルコールを加えてアルコール濃度90体積%以上とし、生じる沈殿を除去して再度液状成分を得ることを特徴とする、シソ抽出液の製造方法。

【請求項2】 シソ科植物を含水率10～30体積%の低級アルコールで抽出し、得られた抽出液を濃縮した後、水を加えてアルコール濃度を10体積%以下にして生じる沈殿を除去し、得られた抽出液を濃縮後、低級アルコールを加えてアルコール濃度90体積%以上とし、生じる沈殿を除去して再度液状成分を得、さらに活性炭を加えて残存する不純分を除去することを特徴とする、シソ抽出液の製造方法。

【請求項3】 シソ科植物がシソ、アオジソ、チリメンジソまたはマンネンロウである請求項1または2記載のシソ抽出液の製造方法。

【請求項4】 シソ科植物を含水率10～30体積%の低級アルコールで抽出し、水を加えて生じる沈殿を除去し、得られた抽出液を濃縮後、低級アルコールを加えてアルコール濃度90体積%以上とし、生じる沈殿を除去することにより得られた、シソ抽出液からなるメラニン生成阻害剤。

【請求項5】 シソ科植物を含水率10～30体積%の低級アルコールで抽出し、得られた抽出液を濃縮した後、水を加えてアルコール濃度を10体積%以下にして生じる沈殿を除去し、得られた抽出液を濃縮後、低級アルコールを加えてアルコール濃度90体積%以上とし、生じる沈殿を除去して再度液状成分を得、さらに活性炭を加えて残存する不純分を除去することにより得られた、シソ抽出液からなるメラニン生成阻害剤。

【請求項6】 シソ科植物がシソ、アオジソ、チリメンジソまたはマンネンロウである請求項4または5記載のメラニン生成阻害剤。

【請求項7】 シソ科植物を含水率10～30体積%の低級アルコールで抽出し、水を加えて生じる沈殿を除去し、得られた抽出液を濃縮後、低級アルコールを加えてアルコール濃度90体積%以上とし、生じる沈殿を除去することにより得られた、シソ抽出液を含有することを特徴とする美白化粧品。

【請求項8】 シソ科植物を含水率10～30体積%の低級アルコールで抽出し、得られた抽出液を濃縮した後、水を加えてアルコール濃度を10体積%以下にして生じる沈殿を除去し、得られた抽出液を濃縮後、低級アルコールを加えてアルコール濃度90体積%以上とし生じる沈殿を除去して再度液状成分を得、さらに活性炭を加えて残存する不純分を除去することにより得られた、シソ抽出液を含有することを特徴とする美白化粧品。

【請求項9】 シソ科植物がシソ、アオジソ、チリメン

ジソまたはマンネンロウである請求項7または8記載の美白化粧品。

【発明の詳細な説明】

【0001】

【産業上の利用分野】本発明は、皮膚の美白、または日焼けやシミ、ソバカス等の皮膚色素沈着の防止・除去に有効なシソ抽出液の製造方法に関し、詳しくはロズマリン酸等を高濃度に含有するシソ特有の色素成分を殆ど含まない、美白化粧品に好適に用いられるシソ抽出液の製造方法に関する。さらには、そのシソ抽出液を皮膚の美白、または日焼けやシミ、ソバカス等の皮膚色素沈着の防止・除去に有効なメラニン生成阻害剤として用いる用途に関し、そして、それを含有する美白化粧品に関する。

【0002】

【従来の技術】従来、シソ科植物から、熱水あるいは液体域の二酸化炭素を用いて抽出液を得る方法が検討されている（特開昭62-65660号、特開昭60-120957号公報）。しかし、これらの方法は、主としてシソ特有の色素成分あるいは香氣成分を損なわずに得ることを目的としており、このような抽出液はシソ特有の色素や糖、タンニン等を多量に含有するために、非常に濃い黄褐色、緑褐色あるいは赤褐色を呈し、特異臭を有している。このような抽出液を化粧品あるいは皮膚外用剤に配合した場合、着色や乳化系の不安定化等の製剤上の問題が生じ、その剤型や配合量がかかなり制約されるとの不都合がある。

【0003】ところで、ロズマリン酸は、シソ、アオジソ、チリメンジソ、ハーブの1種であるローズマリー（マンネンロウ）、セイヨウハッカ、カワミドリ、延命草等のシソ科植物の有効成分として、抗炎症作用、抗アレルギー作用等の薬理効果のあることが、既に知られており、これらの植物は古くから安全性の高い民間薬として利用されている。したがって、上記のシソ科植物を熱水などで抽出した抽出液は、ロズマリン酸を含有しているが、このような抽出液を化粧品あるいは皮膚外用剤に配合して、ロズマリン酸の薬効を利用しようとしても、上記の夾雑成分に由来する着色や乳化系の不安定化等の製剤上の問題があり、そのために、抽出液の配合量に制約があり、化粧品あるいは皮膚外用剤においてロズマリン酸としての薬効を十分に奏する高い濃度で抽出液を添加使用することが困難である。

【0004】こうした背景に基づいて、シソ科植物からロズマリン酸をできるだけ純粋な形で抽出精製して、化粧品に適用する方法が提案されているが（特開昭63-162611号公報）、アセトン、エチルエーテル等の危険な溶剤を用いる抽出工程、カラムクロマト精製の工程等、その操作方法はかなり複雑で、特殊な装置が必要であり、シソ科植物からの抽出精製方法として有利なものではない。

【0005】ところで、日焼けやシミ、ソバカス等の皮膚の色素沈着は、表皮細胞に存在する細胞メラノサイトにおいて生成された色素メラニンが隣接細胞に拡散することで生じる。このメラノサイトでのメラニン生成に中心的役割を果たしている酵素チロシナーゼの生成を抑制することで、あるいは酵素チロシナーゼを直接阻害することで、メラニン生成を抑制する薬剤は種々知られている。従来より用いられてきた代表的な薬剤として、コウシ酸やアルブチンがある。また、酵素チロシナーゼの作用により生じたドーパやドーパキノンから酵素的または非酵素的酸化作用によりメラニンが生成するが、その過程を阻害することで、その生成を抑制する薬剤も、種々知られている。その代表的な薬剤として、アスコルビン酸、ハイドロキノン等がある。しかし、これらのメラニン生成阻害剤は、ヒトに対する毒性・皮膚官能的影響、安定性等を考慮するとき、化粧品原料として必ずしも満足できるものではない。したがって、安定性が高く、安定なメラニン生成阻害剤の開発が望まれている。

【0006】

【発明が解決しようとする課題】以上、従来のシソ抽出液を化粧品あるいは皮膚外用剤に配合する場合に発生する製剤上の問題点や、抽出精製に際しての問題点等に鑑みて、本発明の目的は、シソ〔*Perilla frutescens* (L.) Britton var. *acuta* Kudo〕、アオジソ〔*Perilla frutescens* (L.) Britton var. *acuta* Kudo form *aviridis* Makino〕、チリメンジソ〔*Perilla frutescens* (L.) Britton var. *crispa* (Thunb.) Decne〕、マンネンロウ〔ローズマリー、*Rosmarinus officinalis*〕等のシソ科植物の薬効成分のカフェイン酸、ペリラルデヒド、ロズマリン酸等を高濃度に含有し、しかもシソ特有の濃い黄褐色、緑褐色あるいは赤褐色の色素を殆ど含有しないシソ抽出液と、その新規な工業的に有利な製造方法を提供することにある。併せて、ヒトに対する安全性が高く、極めて優れたメラニン生成阻害剤として用いることのできるシソ抽出液を提供することにある。

【0007】

【課題を解決するための手段】本発明者は、以上の課題を解決するために、下記のような工程を有するシソ抽出液の製造方法を確立し、そのシソ抽出液に酵素チロシナーゼの生成を阻害する作用があり、安全性が高く安定なメラニン生成阻害剤として用いることができることを始めて見だし、本発明を完成した。

【0008】すなわち、本発明によれば、シソ科植物を含水率10～30体積%の低級アルコールで抽出し、得られた抽出液を10体積%以下に濃縮した後、水を加えてアルコール濃度を10体積%以下にして生じる沈殿を

除去し、得られた抽出液を再び10体積%以下に濃縮後、低級アルコールを加えてアルコール濃度90体積%以上とし、析出する沈殿を除去して再度液状成分を回収して抽出液を得、さらに活性炭を加えて攪拌し残存する不純分を除去することにより、目的とするシソ抽出液を得ることができる。このシソ抽出液は、安全性が高く、安定なメラニン生成阻害剤としての用途に用いることができ、美白化粧品に配合することができる。

【0009】さらに詳しくは、本発明で用いられるシソ科植物としては、シソ、アオジソ、チリメンジソ、マンネンロウ（ローズマリー）等が挙げられる。また、メラニン生成阻害作用を有する有効成分を多く含む植物部位として葉茎部がある。採取後生のまま用いてもよいし、天日乾燥等の乾燥処理をしたものを用いても差し支えない。葉茎は、細片状にしたものを使うことが抽出効率上望ましい。チリメンジソの乾燥品として蘇葉が生薬として市販されており、これを用いても差し支えない。

【0010】成分を抽出する含水率10～30体積%の低級アルコール、すなわち含水アルコールの量は、葉茎が浸る量であれば足りるが、シソ科植物の5～15倍重量が好ましい。未乾燥の植物を用いるときは、植物中の水分を考慮して、抽出溶媒のアルコール濃度を高めに設定することが望ましい。低級アルコールとしてはメタノール、エタノール、n-プロパノール、イソプロパノール、t-ブタノール等があるが、好ましくはエタノール、メタノールがよい。抽出溶媒の含水率が10～30体積%を外れると、目的としない成分や色素が突雑してくる。

【0011】抽出操作は、室温で行ってもよいが、好ましくは還流冷却下加熱すると、メラニン生成抑制成分が効率よく速やかに抽出される。抽出圧は常圧でよく、抽出時間は抽出温度により異なるが、2～48時間が望ましい。抽出操作の後、不溶性の残渣を濾過して除去する。成分の抽出操作は残渣についても繰返し行くと、収量を上げることができる。得られた抽出液を減圧濃縮機でもとの抽出液の容積の10体積%以下になるまで濃縮した後、次いで水を加えてアルコール濃度を10体積%以下にし、好ましくは4～10℃で15時間以上静置し、生じる沈殿を濾過等により除去する。得られた液状成分である抽出液を再び10体積%以下に濃縮後、低級アルコールを加えてアルコール濃度90体積%以上とし、好ましくは4～10℃で15時間以上静置し、析出する沈殿を濾過等により除去して再度液状成分を回収して抽出液を得る。この抽出液に対し、0.5～2重量%の活性炭を加えて攪拌し、残存する不純分を除去して、目的とするシソ抽出液を得る。このようにして得られたシソ抽出液は、カフェイン酸、ペリラルデヒド、ロズマリン酸等の物質を含むことが、定性試験により明らかとなった。また、シソ抽出液がメラニン生成阻害作用を有することは、本発明者が始めて見出したものであ

る。

【0012】

【実施例1】シソ抽出液の製造方法

蘇葉（ウチダ和漢）50Kgに80体積％エタノール（含水率20体積％）600Lを加え、40℃に加温下、24時間静置、浸漬抽出を行った。抽出液を濾過後、残渣の蘇葉にさらに600Lの80体積％エタノールを加え、同様の操作をした。2回の抽出液を合わせて1097Lの抽出液（1次抽出液）を得た。この1次抽出液を50℃加温下減圧濃縮し50Lにした後、水100Lを加え10℃にて24時間静置した。生じた不溶性の沈殿物を濾過除去した後、活性炭0.75重量％を加えて1時間攪拌処理した後、これを濾過にて除去した。濾過残渣をさらに3Lの90体積％エタノールで洗浄し、合わせて102Lのシソ抽出液を得た。この蘇葉からのシソ抽出液は、実施例2のチロシナーゼ活性測定試験によれば、メラニン生成抑制阻害作用を示す画分である。（そのチロシナーゼ活性測定試験において、このシソ抽出液を「シソ抽出液」として用いる。）

【0013】

【実施例2】チロシナーゼ活性効果

マウス由来のメラノーマ（黒色腫）細胞B16株を15*

表1 チロシナーゼ生成阻害活性

測定薬剤	作用濃度 μg/ml	チロシナーゼ活性 ΔOD ₄₇₅ /min./mg Protein	阻害率 %	メラニン含量 OD ₄₉₀ /l × 10 ⁴ cells	メラニン生成率 %
コントロール		5.748 × 10 ⁻³	0	1.0320	100
アルブチン	10	1.399 × 10 ⁻³	75.7	0.6210	60.2
	30	0.682 × 10 ⁻³	88.4	0.5050	48.9
コウジ酸	200	9.358 × 10 ⁻⁴	83.7	0.9025	87.5
	400	2.380 × 10 ⁻⁴	95.9	0.6440	62.4
シソ抽出液	3.0	3.618 × 10 ⁻³	37.1	0.5085	48.8
	6.0	2.221 × 10 ⁻³	61.4	0.6470	38.4

【0017】本発明により抽出されたシソ抽出液は、メラノサイトでメラニン生成に中心的役割を果たしている酵素チロシナーゼの生成を阻害する作用を有し、その作用によりメラニン生成の抑制されることが、表1のチロシナーゼ活性測定試験により示されている。その作用 ※50

* 0 cm² の10%ウシ胎児血清含有のイーグルMEM培地30mlを含む動物培養用フラスコに、その細胞密度が2.5 × 10⁴ 細胞/cm² になるように接種し、5%CO₂ 下、37℃にて24時間培養後、下記表1に示す物質を表記の作用濃度になるように各フラスコに添加し、さらに同条件下で3日間培養を行った。

【0014】培養終了後、0.25%トリプシン溶液にて処理し、細胞を収集し、PBS（-）緩衝液10mlで2回洗浄し、その後、0.1%トライトンX100含有0.1Mリン酸緩衝液（pH6.8）2mlに懸濁した。超音波処理後、12000rpmにて20分間遠心して上澄みを得て、チロシナーゼ画分とした。

【0015】チロシナーゼ画分0.5mlと0.05% L-DOPA含有リン酸緩衝液（pH6.8）0.5mlを混合し、室温にて経時的に475nmの吸光度を測定して、その初速度からチロシナーゼ活性を求めた。また、そのチロシナーゼ画分に含まれる総タンパク含有量は、Bio-Rad Protein Assay（バイオラッド社製）のマニュアルに従い測定した。

20 【0016】

【表1】

※は、アルブチンおよびコウジ酸に比較して、極めて低い濃度で、高いチロシナーゼ阻害率、低いメラニン生成率を示す点で特異的である。マンネンロウについて同様の製造方法により抽出された抽出液も、同様にメラニン生成阻害作用を示した。

【0018】

【実施例3】洗顔クリーム

* 実施例1のシソ抽出液を、メラニン生成阻害剤として下

* 記の洗顔クリームの処方(全100重量%)に用いる。

成分A	重量%
ミリスチン酸	14.0
ステアリン酸	12.0
ラウリン酸	3.5
オレイルアルコール	1.5
ヤシ油脂脂肪酸アミドプロピルベタイン	10.5
成分B	重量%
濃グリセリン	18.0
水酸化カリウム	7.0
精製水	残部
防腐剤(パラオキシ安息香酸エステル)	適量
成分C	重量%
シソ抽出液	0.5
香料	0.2

成分Aを加熱溶解し、80℃に保持する。別に80℃に加熱溶解した成分Bを成分Aに加え、充分混合する。攪拌しながら冷却を行い、50℃にて成分Cを加え、洗顔クリームを得た。

※【0019】

【実施例4】化粧水

実施例1のシソ抽出液を、メラニン生成阻害剤として下

※20 記の化粧水の処方(全100重量%)に用いる。

成分	重量%
精製水	残部
濃グリセリン	4.0
ソルビット液(70重量%水溶液)	4.0
クエン酸(pH調整剤)	適量
クエン酸ナトリウム	0.3
ポリオキシエチレン硬化ヒマシ油	0.5
エタノール	15.0
シソ抽出液	1.0
香料	0.05

全成分を室温にて攪拌、混合して均一な溶液としpH 5.5に調節して、化粧水を得た。

★【実施例5】乳液

実施例1のシソ抽出液を、メラニン生成阻害剤として下

★ 記の乳液の処方(全100重量%)に用いる。

【0020】

成分A	重量%
精製水	残部
ショ糖脂肪酸エステル(第一工業製薬S-160)	1.0
濃グリセリン	6.0
防腐剤(パラオキシ安息香酸エステル)	適量
カルボキシビニルポリマー	0.06
水酸化カリウム	0.028
成分B	重量%
オリーブ油	4.0
ホホバ油	4.0
乳酸ミリスチル	2.0
自己乳化型モノステアリン酸グリセリン	1.5
親油型モノステアリン酸グリセリン	1.5
成分C	重量%
シソ抽出液	0.5
香料	0.2

成分Aを加熱溶解し、80℃に保持する。別に80℃に☆50☆加熱溶解した成分Bを成分Aに加え、充分混合する。攪

拌しながら冷却を行い、50℃にて成分Cを加え、乳液を得た。

【0021】

成分A	重量%
精製水	残部
濃グリセリン	6.0
1,3-ブチレングリコール	2.0
防腐剤(パラオキシ安息香酸エステル)	適量
カルボキシビニルポリマー	0.22
水酸化カリウム	0.15
成分B	重量%
スクワラン	7.0
オリーブ油	10.0
ホホバ油	5.0
自己乳化型モノステアリン酸グリセリン	1.5
親油型モノステアリン酸グリセリン	1.5
ポリソルベート60	1.8
モノステアリン酸ソルビタン	0.5
成分C	重量%
シソ抽出液	1.5
香料	0.2

成分Aを加熱溶解し、80℃に保持する。別に80℃に加熱溶解した成分Bを成分Aに加え、充分混合する。攪拌しながら冷却を行い、50℃にて成分Cを加え、クリームを得た。

【0022】以上、シソ科植物から得られたシソ抽出液が、美白成分として洗顔クリーム、化粧水、乳液、クリーム等の化粧品に配合される。その化粧料をヒトに対して適用した結果、皮膚に対する官能的影響は極めて良好であった。

【0023】

【発明の効果】シソ科植物の成分には、抗炎症作用、抗アレルギー作用、鎮痙・鎮痛作用等が知られ、古くから民間薬として利用されているが、それが皮膚の美白、日※

*【実施例6】クリーム

実施例1のシソ抽出液を、メラニン生成阻害剤として下

* 記のクリームの処方(全100重量%)に用いる。

※焼けやシミ、ソバカス等の皮膚色素沈着の防止・除去、メラニン生成抑制の作用を有することは、これまで知られていなかった。本発明により得られる、シソ抽出液は、カフェイン酸、ペリラルデヒド、ロズマリン酸等の成分を含むものであるが、表皮細胞に存在する細胞メラノサイトにおいて色素メラニン生成に中心的役割を果たしている酵素チロシナーゼの生成を抑制する作用があり、その作用によりメラニン生成の抑制されることが、表1のチロシナーゼ活性測定試験の結果から明らかとなった。したがって、このシソ抽出液は、その安全性の点から好ましいばかりでなく、メラニン生成阻害剤として極めて有用であり、それを含有する化粧料は優れた美白効果を有するものである。